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EXAMINER	
FUBARA, BLESSING M	
ART UNIT	PAPER NUMBER
1618	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/763,876	DOMB, ABRAHAM J.	
	Examiner	Art Unit	
	BLESSING M. FUBARA	1618	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *04 February 2008*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-10* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-10* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

The examiner acknowledges receipt of amendment, terminal disclaimer, request for extension of time and remarks, all filed 02/04/08. Claims 11-14 were canceled by the amendment of 7/26/07. Therefore, claims 1-10 are pending.

The claims:

It is brought to applicant's attention that claims 11-14 were canceled by the amendment of 7/26/07 and cancelled claims cannot be brought back with the original numbering. Furthermore, the amendment of 7/26/07 was in response to restriction requirement, so that even if these claims were brought back in the original form, they would have been restricted again as directed to non-elected claims. Also, original claim 1, line 2, recited "polymer" and not "copolymer." In all, the amendment is non-compliant because the status identifier for claim11-14 should read "canceled." Also, "copolymer" in the amended claim 1 should have been underlined to indicate the amendment from "polymer" to "copolymer," while "polymer" should have been canceled using acceptable claim amendment format.

It is suggested that applicant use appropriate status identifier to identify all the claims in the application filed.

Previous rejections that are not reiterated herein are withdrawn.

Claim Rejections - 35 USC § 112

1. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

2. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

3. Claims 1-10 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is new matter rejection.

4. The amendment to claim 1 requires that the biodegradable poly(ester-anhydride) contain random amide bonds. But the specification as filed does not envision biodegradable poly(ester-anhydride) to contain random amide bonds. Applicant has referred to page 8, lines 26 and 27, page 13, lines 1-19, page 15, lines 11-13 and Figure 1 as providing support for the amendment, but while there is support for random ester bonds, but, there is no support for random amide bonds.

This rejection may be overcome by removing the new matter form the claims.

5. Claims 4-7 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

6. Amended claim 1 requires the presence of amide bond in the polymer. But the polyester anhydride structure shown in claim 4 does not have amide bond because R' is ricinoleic acid residue and R'' aliphatic or aromatic moiety; R is also oleic acid, ricinoleic acid or linoleic acid. Thus, because the polyester anhydride does not have a Nitrogen in the copolymer and because R' and R'' do not have a nitrogen that would be contributing to the amide bond in the polymer, it is

unclear how claim 4 would depend on claim 1 when the poly(ester anhydride) has random amide bond.

7. For claims 6 and 7, the dicarboxylic acid from which the copolymer is formed from do not have nitrogen that may contribute to the amide bond in the copolymer. It is unclear therefore, how claims 6 and 7 would depend on claim 1 when the poly(ester anhydride) has random amide bonds.

8. Regarding claim 6, the boundaries of the ester derivatives of ricinoleic acid is not defined.

Response to Arguments

9. Applicant's arguments filed 2/04/2008 have been fully considered but they are not persuasive.

10. Applicant argues that ester derivative is clear because ester derivative of ricinoleic acid is when either of the two functionalities on the acid is esterified, but the meets and bound of that derivative is not known. It was brought to applicant's attention that the specification at paragraph [0049] says that an example of non-linear fatty acid derivative is ricinoleic acid and it is unclear where the boundaries of the ester derivative of ricinoleic acid would be and although applicant talks about esterified functionality on the ricinoleic acid, applicant did not name any of those derivatives. The issue in not just the clarity of what an ester derivative of ricinoleic acid would be but the meets and bounds of those derivatives. Correction is respectfully requested.

Claim Rejections - 35 USC § 102

11. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

12. Claims 1 and 6-8 are rejected under 35 U.S.C. 102(b) as being anticipated by Storey et al. (US 5,756,652).

13. Storey discloses a biodegradable poly(ester anhydride) that are used in medical implants for the release of bioactive substances (abstract; column 1, lines 6-11; column 5, lines 15-22) meeting claim 1. Claims 6-8 are product by process claims and the claims are thus met by the product of Storey. However, Storey synthesizes the poly(ester anhydride) from carboxy-terminated and bis-carboxy-terminated polyesters (abstract; column 1, lines 6-11; column 2; column 3, lines 57-65). It is noted that Storey does not exclude the ester moiety from being random so that randomness of the ester bond would be inherent (see column 7, lines 16-43)

14. Claims 1 and 6-8 are rejected under 35 U.S.C. 102(b) as being anticipated by Griffin et al. (US 4,414,381).

15. Griffin describes polyester anhydride copolymer that conations ester and amide linkages (abstract; columns 1-4) ; the polymers are used as fillers, films and moulding powders (column 6, lines 29-34) and when in compositions contain auxiliary materials such as antioxidants, heat stabilizers, lubricants and fire retardants (column 6, lines 35-38) with the antioxidant meeting the limitation of the biologically active agent of claim 1. Claims 6-8 are product by process claims and the claims are thus met by the product of Griffin. However, Griffin prepares the polyester anhydride copolymers from mixed anhydrides (column 2, lines 16-63; column 3) and from dicarboxylic acids (column 4, line 16 to column 5, line 22) and from polyesteramides and polyamides (column 5, line 28). It is noted that Griffin does not exclude the ester moiety from

being random so that randomness of the ester bond would be inherent (see column 5, lines 23-67 and examples 1-3), since Griffin blends/mixes the anhydrides in the preparation just as the instant specification in Example 4.

16. Claims 1-7 and 10 are rejected under 35 U.S.C. 102(b) as being anticipated by or in the alternative, under 35 U.S.C. 103(a) as obvious over Teomim et al. ("Ricinoleic acid-based biopolymers" in the Journal of Biomedical Materials Research, Vol. 45, Issue 3, pages 258-267, John Wiley & Sons, Inc.) or Domb et al. ("Biopolymers as drug carriers and bioactive macromolecules" in Acta Polymerica, 14 Dec. 1998, Volume 49, Issue 10-11, Pages 526 - 533).

Teomim discloses ricinoleic passed biopolymer derived from ricinoleic acid and maleic or succinic anhydride for the delivery of methotrexate, an anticancer agent (pages 258-267). The methotrexate meets claims 2 and 10. Ricinoleic acid meets the requirements of claims 1, 4, 5 and 8. The succinic anhydride or succinate meets claim 6. Since the composition of Teomim is the same composition as the composition in claim 1, it flows that the composition of Teomim would also be "suitable for administration by injection" as recited in claim 3. The polyanhydride polymer of Teomim contains ester bonds (see structure in Table 1 of page 263). Teomim is silent about the randomness of the ester bonds. Thus, in the alternate, since Teomim is silent as to the randomness of the ester bond within the polymer, the randomness of the ester bond within the polymer would be obvious because the preparation method does not exclude randomness of the bonds and applicant has not factually shown that the bonds in the polymer of Teomim are not random and that ester bonds are absent in the polyanhydride polymer of Teomim.

Domb described biodegradable polyanhydrides derived from ricinoleic acid sebacic acid as drug carriers with nystatin, amphotericin B as small molecules drugs disclosed in the

manuscript (pages 526-533). Since the composition of Domb is the same composition as the composition in claim 1, it flows that the composition of Domb would also be "suitable for administration by injection" as recited in claim 3. Specifically, Domb on page 530, left column at the 3rd full paragraph indicates that the polymer is a copolyester-anhydride. Domb is however silent as to the random nature of the of the ester bond in the polymer. But since Domb prepares the polymer by combining ricinoleic acid and maleic anhydride or succinic anhydride just as the polymer is instantly prepared in paragraph [0127], it would flow that the ester bonds are random. However, in the alternate, since Domb is silent as to the randomness of the ester bond within the polymer, the randomness of the ester bond within the polymer would be obvious because the preparation method does not exclude randomness of the bonds and applicant has not factually shown that the bonds in the polymer of Domb are not random and that ester bonds are absent in the polyanhydride polymer of Domb.

Response to Arguments

17. Applicant's arguments filed 2/4/2008 have been fully considered but they are not persuasive.

18. Applicant has analyzed claims 1 and 11, but claims 11-14 were canceled by the amendment of 7/26/2007 and claims 11-14 are thus not available for examination.

Regarding Teomim: The examiner disagrees with the applicant that the polyanhydride of Teomim does not contain random ester bond because applicant prepares the polyester anhydride by blending PSA and ricinoleic acid in a single bond and if that lead to the formation random ester bonds, then the ester bonds of the polyanhydride of Teomim, which is a product from the

combination of ricinoleic acid and diacid half ester would also contains ester bonds that are random. The polymer on page 263 of Teomim shows the presence of ester bonds. The examiner further disagrees with the applicant as to the method of preparation of the polyester anhydride contributing to structure that is different from that of Teomim because, the claim is not directed to the method of preparing the polyester anhydride and the limitations that applicant argues about are not in the claims. It is also brought to applicant's attention that an amide bond is alternate to ester bond.

Regarding Domb: The examiner disagrees with applicant that Domb does not disclose polyester anhydride with random ester bond because Domb has not excluded random ester bonds and if the mixing process of the diacid and the ricinoleic acid leads to a polymer that has random ester bond, then the mixing of the ricinoleic acid and the anhydrides would also lead to a polymer structure having random ester bonds. Furthermore, applicant has not factually shown that the polymer of Domb does not have an ester bond or does not have random ester bond. Domb on page 530, left column at the 3rd full paragraph names the polymer as a copolyester-anhydride. Furthermore, applicant's argument that the small molecule drugs in Domb are modified by conjugation to dextran and the small molecule drugs of the invention are not modified is not persuasive, because conjugation of the small molecule drugs does not change the drugs since the small molecule drugs are released from the polysaccharide conjugate.

Claim Rejections - 35 USC § 103

19. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person

> having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

20. Claims 1, 2, 3, 9 and 10 are rejected under 35 U.S.C. 103(a) as being unpatentable over Storey et al. (US 5,756,652) in view of Gander et al. (US 5,648,096) or Brem et al. (US 5,626,862).

Storey discloses the use of polyester anhydride as an implant for delivery of bioactive substances (abstract; column 1, lines 6-11; column 5, lines 15-22). Storey does not name any specific bioactive substances. But it is known that many bioactive substances are delivered by implant to the desired sites. For example, Gander describes that biodegradable microcapsules are useful in the delivery of bioactive substances as implants and perenterally administrable microparticles using biodegradable polymers (column 1, lines 28, 29, 35-42). Gander further microcapsules that can include low molecular weight active materials (column 6, lines 7-28), nonsteroidal anti-inflammatory drugs (column 6, lines 29-54), sex hormones (column 6, line 55 to column 7, line 3), and antihistamines (column 7, lines 4-57), with these drugs meeting the limitations of the bioactive agents of claims 2 and 10, the administration mode of parenteral or injection meeting claim 3, and the microparticles meeting claim 9.

Also Brem discloses the use of polymeric implant such as microimplants where microparticles, microspheres and microcapsules encapsulate the drugs (column 11, lines 19-28) with the microparticles meeting claim 9, for the delivery of drugs like anticancer drugs such as paclitaxel and camptothecin (abstract; column 7, lines 19 and 20; column 3, lines 64-67; column 5, lines 8-16) with the anti cancer drugs meeting claims 2 and 10; the drug can be encapsulated within the polymer (column 5, lines 18-20) meeting claim 9; the drug can be administered by subcutaneous injection and/or implantation (column 8. lines 53, 59) meeting claim 3.

Therefore, taking the teachings of the references together, the person of ordinary skill at the time the invention was made would have reasonable expectation of success that the biologically active agents of Brem or Gander would be effectively delivered when incorporated in the polymeric device of Storey.

21. Claims 1 and 8 are rejected under 35 U.S.C. 103(a) as being unpatentable over Teomim et al. ("Ricinoleic acid-based biopolymers" in the Journal of Biomedical Materials Research, Vol. 45, Issue 3, pages 258-267, John Wiley & Sons, Inc.) or Domb et al. ("Biopolymers as drug carriers and bioactive macromolecules" in Acta Polymerica, 14 Dec. 1998, Volume 49, Issue 10-11, Pages 526 - 533).

Teomim and Domb are discussed above as meeting the requirements of claim 1. Each of the references does not disclose the recited %amount of the ricinoleic acid relative to the polymer that would produce the desired polymer that would provide the desired release of the active agent, and in the absence of factual showing, the recited %amount of the ricinoleic acid is not inventive over a prior art reference that describes the same composition that is used as drug carrier and that is silent on the amount of the fatty acid.

22. Claims 1 and 9 are rejected under 35 U.S.C. 103(a) as being unpatentable over Teomim et al. ("Ricinoleic acid-based biopolymers" in the Journal of Biomedical Materials Research, Vol. 45, Issue 3, pages 258-267, John Wiley & Sons, Inc.) or Domb et al. ("Biopolymers as drug carriers and bioactive macromolecules" in Acta Polymerica, 14 Dec. 1998, Volume 49, Issue 10-11 , Pages 526 - 533).

Teomim and Domb are described above as anticipating claim 1. Both Domb and Teomim are silent on the particulate nature of the composition. It is known in the art that

particles used as drug carriers have the advantage of high stability, high carrier capacity in view of the large surface area, possibility of incorporation of hydrophobic and hydrophilic substances, capacity for sustained release and ability for use in variable routes of administration including oral, parenteral and inhalation, all of which aid bioavailability and uptake of active substances by the target sites. Therefore, it would be obvious to prepare the composition of Domb or Teomim in particulate form, microparticle or nanoparticle, with the expectation of deriving the advantages of the use of particles in drug delivery.

Response to Arguments

23. Applicant's arguments filed 2/04/2008 have been fully considered but they are not persuasive.

24. Regarding Teomim: Applicant argues that Teomim does not disclose each and every element of the claims the polyanhydride polymer of Teomim that is formed by melt condensation does not have ester or amide bonds in the polymer chain and it would not be obvious to alter the structure of the polymer to place random ester and amide bonds, so that applicant argues that claims 1 and 8 as amended are not obvious over Teomim.

The examiner disagrees. No alteration of the polyanhydride of Teomim is required and proposed. The difference between Teomim and claim 8 is in the amounts of the ricinoleic acid, which would be obvious to a person of ordinary skill in the art to pursue the preparation of the polymer using amounts of the ricinoleic acid that would produce the polymer that would provide desired release of the active agent. The polymer of Teomim has ester bonds as can be seen in the structure on Table I on page 263 of the reference. But because, Teomim does not exclude random ester bonds in the polymer, applicant cannot exclude randomness of any ester bonds in

the polymer. While Teomim may produce the polyanhydride by melt polymerization, applicant has not provided factual evidence that melt polymerization would lead to polymer that would exclude the presence of ester bonds in the polymer or the presence of random ester bonds in the polymer. Regarding particles in claim 9, Teomim describes the use of microspheres at page 258. Therefore, claims 1, 8 and 9 are rendered obvious by Teomim as described above.

25. Regarding Domb: Applicant argues that Domb does not disclose each and every element of the claims because Domb synthesizes polyanhydrides from non-linear hydrophobic fatty acid esters based on ricinoleic acid, maleic acid and sebacic acid, while the claimed compositions are polyester anhydrides containing random ester bonds and/or amide bonds prepared by reacting a polyanhydride with a polyfunctional organic molecule according to figure 1; that it would not be obvious to alter the structure of the polyanhydride of Domb to place random ester and amide bonds in the backbone to achieve the different structural and physical characteristics associated with the claimed polymer; so that applicant argues that claims 1 and 9 are not rendered by Domb.

The examiner disagrees. No structural alteration is required because Domb specifically names the polymer as copolyester-anhydride at page 530, left column and 3rd full paragraph. The claims are directed to product/composition and not to the process of making the composition/product. Applicant also relies on limitations in the specification when the applicant refers to the figure and to the preparation steps in the specification. Furthermore, Domb does not exclude random ester bond in the polymer and applicant cannot exclude random ester bonds form the polymer of Domb. Furthermore, see Wong et al. (US 5,565,188) at column 1, lines 30-33 as evidence that nanoparticles provide for increased bioavailability. Therefore, claims 1, 8 and 9 are rendered obvious by Domb.

26. No claim is allowed.

27. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to BLESSING M. FUBARA whose telephone number is (571)272-0594. The examiner can normally be reached on 7 a.m. to 5:30 p.m. (Monday to Thursday).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael G. Hartley can be reached on (571) 272-0616. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

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